REMARKS

Applicants thank the Examiner for her careful review of the response mailed on November 24, 2003 in response to the Office Action dated May 27, 2003, and the response mailed on February 23, 2004 in response to the subsequent Communication mailed on February 5, 2004. In the most recent Communication from the Examiner mailed on April 30, 2004, the Examiner indicates that the response mailed on November 24, 2003 is still non-responsive to the Office Action dated May 27, 2003, because Applicants failed to provide a SEQ ID NO in new claim 191. Applicants have corrected this inadvertent error by amending claim 191 herein, as suggested by the Examiner.

Based on the Communications from the Examiner dated April 30, 2004 and February 23, 2004, it appears that the Amendment dated November 24, 2003 has not yet been entered. **To eliminate any possible confusion and to expedite prosecution and facilitate the Examiner's review, Applicants hereby submit this present Amendment, which includes the substance of the Amendment mailed on November 24, 2003 and all of the changes suggested by the Examiner in the two subsequent Communications.**

In the event that the Examiner finds any additional inadvertent errors or oversights with this response, Applicants respectfully request that the Examiner telephone the undersigned at (650) 298-5809 so that any such errors or oversights can be corrected immediately.

I. STATUS OF THE CLAIMS.

In the previous response, Applicants elected Group II (claims 37-62, 84, 123-148 and 170) pursuant to an Examiner's restriction requirement and elected SEQ ID NO:8 pursuant to the sequence election requirement. Previously, claims 1-36, 63-83, 85-122, 149-169, and 171-183 were withdrawn from consideration as being drawn to non-elected groups, and claims 123-148 and 170 were withdrawn from consideration as being drawn to non-elected subject matter

pursuant to a restriction requirement. In the Office Action dated May 27, 2003, the Examiner considered claims 37-62 and 84.

Presently, Applicants have canceled claims 1-183 with entry of this amendment without prejudice to subsequent renewal, including in a divisional or continuation application. Applicants have added new claims 184-203. Each of claims 184-208 is supported by the specification as filed and no new matter is added by any of these new claims. Applicants note that claims 37-62 and 84 have been canceled and new claims 184-208 have been added, in part, to conform the pending claims to the restriction requirement and sequence election as suggested by the Examiner.

New claim 184 specifies an isolated or recombinant polypeptide, wherein the polypeptide induces proliferation of T cells in the presence of a p35 polypeptide subunit of human interleukin-12, and wherein the polypeptide comprises a sequence that is at least 95% identical to the mature domain of SEQ ID NO:8. Support for claim 184 is provided throughout the specification, including at, but not limited to, e.g., original claims 37 and 40 and page 3, lines 1-21. New claim 185 specifies the isolated or recombinant polypeptide of claim 184, wherein the mature domain comprises amino acid residues 23-324 of SEQ ID NO:8. Support for claim 185 is provided throughout the specification, including at, but not limited to, e.g., original claim 38.

New claim 186 specifies the isolated or recombinant polypeptide of claim 184, wherein the polypeptide comprises a sequence that is at least 97% identical to the mature domain of SEQ ID NO:8. Support for this claim is provided throughout the specification, including at, but not limited to, e.g., page 3, lines 1-21. New claim 187 specifies the isolated or recombinant polypeptide of claim 186, wherein the polypeptide comprises the mature domain of SEQ ID NO:8. Support for this claim is provided throughout the specification, including at, but not limited to, e.g., page 3, lines 1-21 and original claim 38.

New claim 188 specifies an isolated or recombinant polypeptide, wherein the polypeptide induces proliferation of T cells in the presence of a p35 polypeptide subunit of human interleukin-12, and wherein the polypeptide comprises a sequence that is at least 95%

identical to the sequence of SEQ ID NO:8. New claim 189 specifies the isolated or recombinant polypeptide of claim 188, wherein the polypeptide comprises a sequence that is at least 97% identical to the sequence of SEQ ID NO:8. New claim 190 specifies the isolated or recombinant polypeptide of claim 189, wherein the polypeptide comprises the sequence of SEQ ID NO:8. Support for claims 188-190 is provided throughout the specification, including at, but not limited to, e.g., original claim 37 and page 3, lines 1-21.

New claim 191 is directed to an isolated or recombinant polypeptide which induces proliferation of T cells in the presence of a p35 polypeptide subunit of human interleukin-12, said isolated or recombinant polypeptide comprising a polypeptide sequence (amino acid residue positions 23-238 of SEQ ID NO:39): IWEL-X_{27}-K-X_{29}-VYVVELDWYP-X_{40}-APGE-X_{45}-VVL-X_{49}-CDTPEEDGITWT-X_{62}-DQSS-X_{67}-VLG-X_{71}-GKTLTI-X_{78}-VKEFGDAGQYTC-X_{91}-KGG-X_{95}-X_{96}-LS-X_{99}-SLLLLHKKEDGIWSTDILKDQK-X_{122}-PK-X_{125}-K-X_{127}-FL-X_{130}-CEAK-X_{135}-YSG-X_{139}-FTCWWLT-X_{147}-ISTDL-X_{153}-F-X_{155}-VKSSRGS-X_{163}-DP-X_{166}-GVTCG-X_{172}-X_{173}-X_{174}-LS-X_{177}-X_{178}-X_{179}-X_{180}-X_{181}-X_{182}-X_{183}-X_{184}-X_{185}-X_{186}-X_{187}-X_{188}-Y-X_{190}-VECQE-X_{196}-SACP-X_{201}-AEESLPIEV-X_{211}-X_{212}-X_{213}-A-X_{215}-HKLKYENYTS-X_{226}-FFIRDIIKPDPPKNLQL-X_{244}-PLKNSR-X_{251}-VE-X_{254}-X_{255}-W-X_{257}-YPDTWS-X_{264}-PHSYFSLTF-X_{274}-X_{275}-QVQG-X_{280}-X_{281}-KRE-X_{285}-X_{286}-X_{287}-X_{288}-X_{289}-F-X_{291}-D-X_{293}-TSA-X_{297}-V-X_{299}-C-X_{301}-K-X_{303}-A-X_{305}-I-X_{307}-V-X_{309}-A-X_{311}-DRY-X_{315}-SS-X_{318}-WS-X_{321}-WASV-X_{326}-X_{327}-X_{328}, or a conservatively substituted variation thereof, where X_{27} is K or E; X_{29} is D or N; X_{40} is D or N; X_{45} is M or T; X_{49} is T or A; X_{62} is S; X_{67} is E or G; X_{71} is T; X_{78} is H; X_{91} is H or R; X_{95} is E, A, K, or T, X_{96} is V or A; X_{99} is R or Q; X_{122} is E or K; X_{125} is N or A; X_{127} is S or I; X_{130} is K; X_{135} is N or D; X_{139} is R or H; X_{147} is T or A; X_{153} is T or K; X_{155} is S or T; X_{163} is S or T; X_{166} is Q, R, or H; X_{172} is A or T; X_{173} is A or V; X_{174} is T or L; X_{177} is A or E; X_{178} is E or D; X_{179} is R, L, or K; X_{180} is V or G; X_{181} to X_{184} inclusive is deleted, or is replaced with the sequence S-(L or M)-(E or D)-H-R; X_{185} is E; X_{186} is Y; X_{187} is K or N; X_{188} is K; X_{190} is R or T; X_{196} is G; X_{201} is A or S; X_{211} is V; X_{212} is V or L; X_{213} is D or E; X_{215} is V or I; X_{226} is S or R; X_{244} is K or R; X_{251} is Q or H; X_{254} is V or I; X_{255} is S or N; X_{257} is E or G; X_{264} is T or A; X_{274} is C or G; X_{275} is V or I; X_{280} is K or R; X_{281} is S or N; X_{285} is K or D; X_{286} is K or R;

X_{287} is D or is deleted; X_{288} is R or is deleted; X_{289} is I or L; X_{291} is T or M; X_{293} is K or Q; X_{297} is T or K; X_{299} is I, T, or V; X_{301} is R or H; X_{303} is N or D; X_{305} is K; X_{307} is R; X_{309} is Q; X_{311} is R; X_{315} is Y or H; X_{318} is S or F; X_{321} is E or D; X_{326} is P or S; X_{327} is C or L; and X_{328} is S, G, or Q. Support for new claim 191 is provided throughout the specification, including at, but not limited to, e.g., original claim 45.

New claim 192 specifies an isolated or recombinant polypeptide which induces proliferation of T cells in the presence of a p35 polypeptide subunit of human interleukin-12, wherein the polypeptide comprises a sequence which differs from the mature domain of p40 polypeptide subunit of human interleukin-12 set forth in SEQ ID NO:15 in 1 to 18 amino acid positions and which comprises the substitution Ser305Lys relative to SEQ ID NO:15. Support for claim 192 is provided throughout the specification, including at, but not limited to, e.g., original claims 41, 42, and 44 and page 3, line 22 to page 4, line 4.

New claim 193 specifies the isolated or recombinant polypeptide of claim 192, wherein the polypeptide further comprises a deletion of amino acid residues Arg181 to Asn184 inclusive relative to SEQ ID NO:15. Support for claim 193 is provided throughout the specification, including at, but not limited to, e.g., original claim 41.

New claim 194 specifies the isolated or recombinant polypeptide of claim 192, wherein the polypeptide further comprises at least one substitution relative to SEQ ID NO:15 selected from the group of Leu62Ser, Ser71Thr, Gln78His, His99(Arg or Gln), Thr127(Ser or Ile), Arg130Lys, Lys185Glu, Glu186Tyr, Tyr187(Lys or Asn), Glu188Lys, Ser190(Arg or Thr), Asp196Gly, Met211Val, Val289(Ile or Leu), Ser305Lys, Ser307Arg, Arg309Gln, and Gln311Arg. Support for claim 194 is provided throughout the specification, including at, but not limited to, e.g., original claim 42.

New claim 195 denotes the isolated or recombinant polypeptide of claim 193, wherein the polypeptide further comprises at least one substitution relative to SEQ ID NO:15 selected from the group of Leu62Ser, Ser71Thr, Gln78His, His99(Arg or Gln), Thr127(Ser or Ile), Arg130Lys, Lys185Glu, Glu186Tyr, Tyr187(Lys or Asn), Glu188Lys, Ser190(Arg or Thr), Asp196Gly, Met211Val, Val289(Ile or Leu), Ser305Lys, Ser307Arg, Arg309Gln, and

Gln311Arg. Support for claim 195 is provided throughout the specification, including at, but not limited to, e.g., original claim 42.

New claim 196 specifies the isolated or recombinant polypeptide of claim 194, wherein the polypeptide further comprises the following substitutions relative to SEQ ID NO:15: Lys185Glu, Glu186Tyr, Tyr187(Lys or Asn), Glu188Lys, Ser190(Arg or Thr). Support for claim 196 is provided throughout the specification, including at, but not limited to, e.g., original claim 42.

New claim 197 specifies the isolated or recombinant polypeptide of claim 195, wherein the polypeptide further comprises the following substitutions relative to SEQ ID NO:15: Lys185Glu, Glu186Tyr, Tyr187(Lys or Asn), Glu188Lys, Ser190(Arg or Thr). Support for claim 197 is provided throughout the specification, including at, but not limited to, e.g., original claim 42.

New claim 198 specifies the isolated or recombinant polypeptide of claim 192, wherein the polypeptide further comprises substitutions His99Arg and Val289Ile relative to SEQ ID NO:15. Support for claim 198 is provided throughout the specification, including at, but not limited to, e.g., original claim 42.

New claim 199 recites the isolated or recombinant polypeptide of claim 193 wherein the polypeptide further comprises substitutions His99Arg and Val289Ile relative to SEQ ID NO:15. Support for claim 199 is provided throughout the specification, including at, but not limited to, e.g., original claim 42.

New claim 200 provides for the isolated or recombinant polypeptide of claim 192, wherein the polypeptide further comprises at least one substitution relative to SEQ ID NO:15 selected from the group of Met45Thr, Val96Ala, Glu257Gly, Val275Ile, and Ser318Phe. Support for claim 200 is provided throughout the specification, including at, but not limited to, e.g., original claim 43.

New claims 201, 202, and 203 specify a composition comprising the polypeptide of claim 184, 191, and 193, respectively, and a carrier. Support for these claims is provided throughout the specification, including at, but not limited to, e.g., original claim 58.

New claims 204, 205, and 206 specify compositions of claims 201, 202, and 203, respectively, which further comprise a p35 polypeptide subunit of human interleukin-12. Support for these claims is provided throughout the specification, including at, but not limited to, e.g., original claim 59.

New claim 207 specifies the composition of claim 201, wherein the carrier is a pharmaceutically acceptable carrier. Support for this claim is provided throughout the specification, including at, but not limited to, e.g., original claim 61.

New claim 208 specifies the isolated or recombinant polypeptide of claim 184, wherein the polypeptide induces a 4-fold increase in the proliferation of T cells in the presence of the p35 polypeptide subunit of human interleukin-12 compared to the proliferation of T cells induced by a p40 polypeptide subunit of human interleukin-12 in the presence of the p35 polypeptide subunit of human interleukin-12. Support for this claim is provided throughout the specification, including at, but not limited to, e.g., page 30, line 26, to page 40, line 20. Applicants note that the nucleic acid and polypeptide sequences of clone C2-22 are designated as SEQ ID NO:1 and SEQ ID NO:8, respectively, in the specification. See, e.g., pages 142 and 144 of the specification.

II. OBJECTION TO THE SPECIFICATION AND AMENDMENTS TO THE SPECIFICATION.

Pursuant to a suggestion by the Examiner, the title of the invention has been changed on the title page and the first page of the specification to read "Cytokine Polypeptides."

The Examiner states that the "application fails to comply with the requirements of 37 CFR § 1.821 through 1.825, because the SEQ ID Nos cited along with each sequence in the specification." Office Action, page 3. *Applicants respectfully note that this sentence appears incomplete and thus it is unclear exactly to what the Examiner is referring.* The Examiner states that Applicants are required to submit a new computer readable form sequence listing, a paper copy or CD-ROM for the specification, and statements under 37 CFR § 1.821(f) and (g), if there is a need to list additional sequences in the sequence listing. *Id.* at pages 3-4. The Examiner cites a sequence set forth in the specification on page 109 (line 27) to page 110 (line 5). *Id.* at

pages 3-4. *Given the reference to this particular sequence, it appears the Examiner wishes Applicants to amend the specification to include sequence identifiers for specific fragments of properly presented and identified sequences.* Applicants have done so in an effort to comply with the Examiner's concerns. For example, the paragraph in the specification beginning at page 109, line 26 has been amended to specify further that the sequence shown in the paragraph is identified as amino acid residue positions 23-328 of SEQ ID NO:39. SEQ ID NO:39 is set forth in the previously submitted Sequence Listing. Language such as amino acid residue positions 23-328 of SEQ ID NO:39 is permissible and the fragment need not be separately presented in the Sequence Listing. See, e.g., MPEP § 2422.03. Additionally, in the same paragraph, the specification has been amended in the same paragraph to indicate the N-terminal leader sequence M-X_2-X_3-QQLV-X_8-SWFSLV-X_{15}-LASPL-X_{21}-A represents amino acid residue positions 1-22 of SEQ ID NO:39. The paragraph beginning on page 110, line 26 has been similarly modified. Withdrawal of the objection is respectfully requested.

The specification was objected to because it allegedly contains an embedded hyperlink and/or other form of browser-executable code "on page 46, line 31 and elsewhere." Office Action, page 4. This objection is traversed in part and overcome in part. Applicants do not intend that this web address be an active link in any related published patent or published application. Thus, this link can be disabled by the Office when preparing the text to be loaded onto the USPTO web database. As indicated in MPEP § 608.01, where Applicants do not intend a hyperlink to be an active link (*i.e.*, such that the link becomes a live web link in the published patent or published application when placed on the USPTO web page), the Examiner should not object to the hyperlink and the hyperlink need not be deleted from the specification because the Office can disable the hyperlink when preparing the text to be loaded onto the USPTO web page. Nevertheless, in an effort to expedite prosecution, Applicants have amended the specification to remove web addresses set forth in the described format. Withdrawal of the rejection is respectfully requested.

The specification was also objected to as containing typographical errors on pages 2 and 13. Office Action , page 4. Applicants thank the Examiner for her close review of the

specification. Applicants have amended the specification to correct these inadvertent typographical errors. Applicants have also amended the specification to correct additional inadvertent typographical errors of which they have become aware. None of these amendments introduces any new matter; these amendments are merely undertaken to correct inadvertent typographical errors.

III. OBJECTION TO THE CLAIMS.

Claims 62 and 84 were objected to because of the use of the trademark GENBANK. The Examiner notes that this term should be capitalized and accompanied by the generic terminology. This objection has been rendered moot by cancellation of these claims.

Claims 37-39, 47-48, 50-51, 62, and 84 were objected to as allegedly including subject matter "which has been non-elected due to restriction requirement and therefore withdrawn from consideration." Office Action, page 5. Claims 40, 49 and 52-61 were also objected to due to their direct or indirect dependence from claims 37 and 48. These objections have been overcome by the amendments to the claims.

IV. REJECTIONS UNDER 35 USC § 101.

Claims 48-57, 62, and 84 were rejected under 35 USC § 101 as allegedly directed to non-statutory subject matter. Specifically, the Examiner finds that claims 48-57, 62, and 84 do not sufficiently distinguish over polypeptides as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products." Office Action, page 5. Although Applicants respectfully traverse this rejection, the rejection has been rendered moot by cancellation of these claims.

V. REJECTIONS UNDER 35 USC § 112, FIRST PARAGRAPH.

Claims 62 and 84 were rejected under 37 USC § 112, first paragraph as allegedly failing to comply with the enablement requirement. Specifically, the Examiner finds that the claims contain subject matter which was not described in the specification in such a way as to

enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Office Action, page 6. The Examiner is of the view that the reference to GenBank accession numbers in claims 62 and 84 is an attempt to incorporate essential subject matter and that "[e]nablement of essential subject matter for the practice of claims cannot be properly supplied by incorporation by reference." Office Action, page 7. This rejection has been mooted by cancellation of these claims.

Claims 45-62 were rejected under 37 USC § 112, first paragraph as allegedly "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time of the invention was filed [sic], had possession of the claimed invention." Office Action, page 7 (emphasis added). The Examiner further states that "claims 45-62 are directed to encompass sequences that have a recited degree of identity, sequences that hybridize to SEQ ID NO:1, and modified sequences which do not meet the written description requirement provision of 35 U.S.C. 112, first paragraph." *Id.* The Examiner takes the position that the "90% amino acid sequence identity" as recited in claim 45 (line 2) "could also contain sequences including the entire sequence of SEQ ID NO:8 plus up to 10% additional sequence on either end of SEQ ID NO:8 which fails to meet the written description provision of 35 U.S.C. 112, first paragraph." *Id.* at pages 7-8. The Examiner finds that the specification provides insufficient written description to support the genus encompassed by claims 45-62. Although Applicants respectfully traverse this rejection, the rejection has been rendered moot by cancellation of claims 45-62.

Applicants note that the specification provides clear and sufficient written description to support new claims 184-208. New independent claims 184 and 188 include language specifying a particular degree of percent identity. For example, new claim 184 is specifies an isolated or recombinant polypeptide, wherein the polypeptide induces proliferation of T cells in the presence of a p35 polypeptide subunit of human interleukin-12, and wherein the polypeptide comprises a sequence that is at least 95% identical to the mature domain of SEQ ID NO:8. Notably, claim 184 is limited to those polypeptides which possess the specified function and percent identity. Procedures for making and identifying polypeptides which have the

requisite structural identity and particular function are described in the specification and/or are conventional in the art. Based upon the detailed information and guidance provided in the specification, one of ordinary skill in the art would conclude that Applicants were in possession of the necessary common attributes possessed by members of the genus defined by the claim. Similar reasoning applies to new claim 188.

Applicants respectfully point the Examiner to the USPTO's "Synopsis of Application of Written Description Guidelines," Example 14. Example 14 of the USPTO's "Synopsis of Application of Written Description Guidelines" provides guidance to Examiners on the written description requirement as it pertains to claims that include percent identity language. Additionally, Example 14 explains that "comprising" language is permissible in claims specifying a "protein which comprises SEQ ID NO:3 or a variant thereof that has 95% identity to SEQ ID NO:3." As explained in the Guidelines in this Example, the claimed protein may be larger than SEQ ID NO:3 or its variant with 95% identity to SEQ ID NO:3. For at least these reasons, Applicant submit that new independent claims 184 and 188, as well as claims dependent thereon, clearly satisfy the written description requirement under 35 USC § 112 first paragraph.

Applicants also submit that new independent claims 191 and 192, and claims dependent thereon, satisfy the written description requirement under 35 USC § 112, first paragraph.

VI. REJECTIONS UNDER 35 USC § 112, SECOND PARAGRAPH.

Claims 39-40, 46, 48-62, and 84 were rejected under 35 USC § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. Office Action, page 9. Specifically, the Examiner finds that claims 40, 46, 52, 54, 57, 59, 62, and 84 are vague and indefinite due to the unclarity of citing an abbreviation with a word, such as p35, GST, Met, PEGylated, and p40. *Id.* The Examiner suggests the full name of each such term be included in parentheses in each respective claim. This rejection has been mooted by cancellation of these claims.

Applicants note that newly submitted claims include the phrase "p35 polypeptide subunit of human interleukin-12" instead of simply "p35 polypeptide." See, e.g., new claim 184. This phrase is clear and definite and would be entirely understood by one of ordinary skill in the art, as is shown, e.g., in the references cited by the Examiner.

Similarly, new claims 192 and 208 include the phrase "p40 polypeptide subunit of human interleukin-12" instead of simply "p40 polypeptide." This phrase is also clear and definite and would be fully understood by one of ordinary skill in the art as in the references cited by the Examiner.

The Examiner also finds that the phrase "corresponding to" in claims 39 and 62 is vague and indefinite. This rejection has been mooted by cancellation of these claims.

The Examiner further finds that the phrase "T-cell proliferative activity" in claims 40 and 52 is vague and indefinite. This rejection has been mooted by cancellation of these claims.

The Examiner takes the position that the phrase "encodes a first polypeptide" in claim 48 is vague and indefinite. This rejection has been mooted by cancellation of this claim.

Claims 49-61 were rejected due to their direct or indirect dependence from claim 48. This rejection has been mooted by cancellation of these claims.

The Examiner is of the view that the phrase "secretion/localization sequence" in claim 53 is vague and indefinite. Claim 54 was rejected due to its dependency from claim 53. This rejection has been mooted by cancellation of these claims.

VII. REJECTIONS UNDER 35 USC § 102.

Claims 37, 40-46, and 55-59 were rejected under 35 USC § 102(b) as allegedly being anticipated by Foss *et al.*, *Vet. Immunol. Immunopathol.* 57:121-134 (1997) [hereinafter "Foss"]. Specifically, the Examiner finds that "Foss discloses a nucleic acid (Figure 1) that encodes a polypeptide which is 90.7% identical to SEQ ID NO:8 as stated in claim 37 as defined by claims from which it depends" and Foss also "discloses a p40 polypeptide (Figure 2B(p)) which contains modifications at equivalent positions of SEQ ID NO:15 of the instant invention

(Figure 2B (h))." Office Action, page 10. This rejection has been mooted by cancellation of these claims.

Applicants respectfully submit that none of new claims 184-208 is anticipated by Foss. For example, new independent claim 184 is directed to an isolated or recombinant polypeptide, wherein the polypeptide induces proliferation of T cells in the presence of a p35 polypeptide subunit of human interleukin-12, and wherein the polypeptide comprises a sequence that is at least 95% identical to the mature domain of SEQ ID NO:8. New independent claim 188 specifies an isolated or recombinant polypeptide, wherein the polypeptide induces proliferation of T cells in the presence of a p35 polypeptide subunit of human interleukin-12, and wherein the polypeptide comprises a sequence that is at least 95% identical to the sequence of SEQ ID NO:8. Neither claim 184 nor claim 188 is anticipated by the teachings of Foss, because Foss does not teach or suggest all of the limitations of either such claim. Foss merely discloses the sequence of porcine IL-12. Foss does not disclose an isolated or recombinant polypeptide sequence that possesses the particularly defined functional property and has at least 95% identity to SEQ ID NO:8 or the mature domain thereof.

New claim 191 is also not anticipated by the teachings of Foss. Claim 191 specifies a sequence that is not taught or suggested by the porcine IL-12 sequence set forth in Foss. The particular sequence explicitly defined by claim 191, for example, requires, among other things, a D residue at position 51, a T residue at position 272, a T residue at position 294, an R residue or deletion of the residue at position 288, and a K residue at position 305, and an S, G, or Q residue at position 328. None of these residues is present at an equivalent position in porcine IL-12.

New claim 192 is similarly not taught or suggested by the teachings of Foss. Claim 192 specifies an isolated or recombinant polypeptide which induces proliferation of T cells in the presence of a p35 polypeptide subunit of human interleukin-12, wherein the polypeptide comprises a sequence which differs from the mature domain of p40 polypeptide subunit of human interleukin-12 set forth in SEQ ID NO:15 in 1 to 18 amino acid positions and which comprises the substitution Ser305Lys relative to SEQ ID NO:15. Foss discloses only the

sequence of porcine IL-12. Foss does not teach or suggest the specific polypeptide particularly defined by claim 192.

For at least these reasons, Applicants submit that the new claims 184, 188, 191, and 192 (as well as new claims dependent thereon) are not anticipated by the teachings of Foss.

Claims 37 and 40 were rejected under 35 USC § 102(b) as allegedly being anticipated by Paoletti *et al.* (US Pat. No. 5,833,975) [hereinafter "Paoletti"]. The Examiner finds that Paoletti "discloses a nucleotide sequence of a p40 expression cassette (SEQ ID NO:194) which encodes a polypeptides which is 88.5% identical to SEQ ID NO:8 as stated in claim 37 as defined by claims from which it depends." Office Action, page 11. The Examiner also finds that Paoletti discloses "cytokine interleukin 12 (IL-12) is a heterodimer composed of 35 kDa and 40 kDa subunits which plays a major role in promoting the T_H1 cell mediated immune response by T-cell proliferative activity (col. 14, lines 4-8 and 47-54) as stated in claim 40." *Id.* The Examiner further finds that Paoletti discloses "recombinant vaccinia virus expressing IL-12 (modified) is attenuated in mice compared to wild-type vaccinia virus due to the ability of the vaccinia-expressed IL-2 to stimulate mouse NK cells to produce IFN-gamma (col. 14, lines 11-16). *Id.* at pages 111-12. Based on these findings, the Examiner concludes that Paoletti anticipates claims 37 and 40.

Although Applicants traverse the Examiner's rejection, this rejection has been mooted by cancellation of claims 37 and 40.

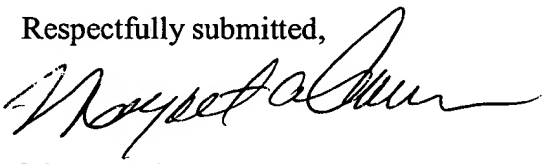
Furthermore, Applicants respectfully submit that none of claims 184-208 is anticipated by Paoletti's teachings. Paoletti merely discloses the polypeptide sequence of the p40 subunit of human IL-12. Paoletti does not teach or suggest all of the limitations of any of the new claims, each of which specifies a novel isolated or recombinant polypeptide which comprises a particularly specified sequence and which induces proliferation of T cells in the presence of a p35 polypeptide subunit of human IL-12.

CONCLUSION

In the event that the Examiner finds any additional inadvertent errors or oversights with this response, Applicants respectfully request that the Examiner telephone the undersigned at (650) 298-5809 at her earliest convenience so that any such errors or oversights can be corrected immediately.

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Respectfully submitted,



Margaret A. Powers
Reg. No. 39,804

May 24, 2004
Maxygen, Inc.
Intellectual Property Department
515 Galveston Drive
Redwood City, California 94063
Telephone: (650) 298-5809
Facsimile: (650) 298-5446
Customer No. 30560